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| 10/582,027 | 06/08/2006 | Maria Dorly Del Curto | SER-111 | 1354 |

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| EXAMINER | |
|---|---|
| HISSONG, BRUCE D | |

| ART UNIT | PAPER NUMBER |
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| 1646 | |

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| 01/25/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

euspto@slspatents.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/582,027 | DEL CURTO, MARIA DORLY | |
| | Examiner | Art Unit | |
| | Bruce D. Hissong, Ph.D. | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-15,17-23,25 and 32-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15, 17-23, 25, 32-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 October 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/14/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

***Formal Matters***

1. Applicant's response to the office action mailed on 6/23/209, including arguments/remarks and amended claims, drawings, and specification, was received on 10/14/2009 and has been entered into the record.

2. In the response received on 10/14/2009, the Applicant cancelled claims 16 and 24, and added new claims 38-44. Claims 1-15, 17-23, 25, and 32-44 are pending, and are the subject of this office action.

***Information Disclosure Statement***

The information disclosure statement received on 10/14/2009 has been fully considered.

***Drawings***

Objection to the drawings, as set forth on page 2 of the office action mailed on 6/23/2009, is *withdrawn* in view of Applicants submission of new replacement drawings.

***Specification***

Objection to the specification for containing an embedded hyperlink, as set forth on page 2 of the office action mailed on 6/23/2009, is *withdrawn* in view of Applicants amendments to the specification.

***Claim Objections***

1. Objection to claims 1 and 32, as set forth on page 2 of the office action mailed on 6/23/2009, is *withdrawn* in view of Applicants amendments to claim 1 to recite and define the acronym HPBCD.

2. Objection to claims 12-14, as set forth on page 2 of the office action mailed on 6/23/2009, is *withdrawn* in view of Applicants amendments to the claims to recite "said antioxidant".

3. Objection to claim 33 for failing to further limit the subject matter of a previous claim, as set forth on page 3 of the office action mailed on 6/23/2009, is *withdrawn* in view of Applicants amendments to the claim to recite only mono-dose administration.

***Claim Rejections - 35 USC § 112, first paragraph – written description***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejection of claims 1-15, 17-23, 25, and 32-27 under 35 USC § 112, first paragraph, regarding lack of written description for the genus of interferon (IFN) isoforms, muteins, fused proteins, functional derivatives, active fractions, or salts thereof, as set forth on pages 3-4 of the office action mailed on 6/23/2009, is *withdrawn* in response to Applicant's amendments to the claims to delete these limitations from the claims.

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Rejection of claims 21-22 under 35 USC § 112, second paragraph, regarding lack of antecedent basis for the limitation "said bacteriostatic agent" of claim 18, as set forth on page 4 of the office action mailed on 6/23/2009, is *withdrawn* in response to Applicant's amendments to claims 21-22 to depend from claim 19, rather than claim 18.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

1. Claims 1-11, 13-15, 17-19, 21-22, and 25 *remain rejected*, and new claims 39-41 are also rejected under 35 USC § 103(a) as being obvious in view of the combination of Shirley *et al* ("Shirley" – US 20020172661) and Dorin *et al* ("Dorin" – US 5,814,485), as set forth on pages 5-7 of the office action mailed on 6/23/2009.

The claims of the present invention are drawn to stabilized pharmaceutical compositions comprising an IFN, and further comprising a buffer, 2-hydroxypropyl-beta-cyclodextrin (HPBCD), an isotonicity agent, and an anti-oxidant, wherein the HPBCD is present at about 500-fold to about 700-fold molar excess with respect to said IFN. The claims are further drawn to compositions comprising IFN-β at various concentrations, including recombinant IFN-β, and buffers, and specifically acetate buffer, at various concentrations and in an amount sufficient to maintain the pH of the composition within plus or minus 0.5 units of a specified pH, wherein the specified pH is about 3 to about 6. The claims also specifically recite mannitol as the isotonicity agent at various concentrations.

Shirley teaches stabilized liquid (i.e. aqueous) formulations of IFN-β (paragraphs 0002, 0039), including recombinant IFN-β (see claim 32) in a solution with a buffer, wherein the buffer is in an amount sufficient to maintain the pH of the composition within plus or minus 0.5 units of a specified pH, wherein the specified pH is about 3.0 to about 5.0 (see claim 1), and wherein the IFN-β concentration can range from 0.01 mg/ml to 20 mg/ml (10 μg/ml - 20,000 μg/ml - paragraph 0069) Shirley teaches numerous suitable buffers, including acetate buffer at a concentration range of 1 - 30 mM (paragraph 0034). Shirley also teaches that this composition can further comprise a "tonicifying agent" such as mannitol (paragraph 0038). Also disclosed is the inclusion of EDTA (paragraph 0072), disclosed as an agent that "acts as a scavenger of metal ions known to catalyze many oxidation reactions" and which the present specification lists as a suitable anti-oxidant. Shirley also teaches inclusion of bacteriostatic agents (paragraph 0048). Therefore, Shirley teaches a liquid composition comprising recombinant IFN-β which may comprise a buffer (acetate buffer), an isotonicity agent (mannitol), and an anti-oxidant (EDTA), as well as bacteriostatic agents. Shirley is silent regarding a stabilized composition comprising 2-hydroxypropyl-beta-cyclodextrin.

However, Dorin teaches compositions comprising IFN-β, and teaches that these IFN-β formulations can comprise 2-hydroxypropyl-beta-cyclodextrin, and also teaches that inclusion of 2-hydroxypropyl-beta-cyclodextrin is useful as a protectant because helps reduce the physical and chemical alterations to IFN-β polypeptides, such as oxidation. Dorin also teaches that 2-hydroxypropyl-beta-cyclodextrin helps prevent unwanted aggregation, chemical linkage, oxidation, and degradation of IFN-β (column 13, lines 6-31, and especially lines 21-31).

In the response received on 10/14/2009, the Applicant argues that the presently claimed invention is not obvious in view of the combination of Shirley and Dorin because the claims have been amended to recite a stabilized liquid pharmaceutical composition comprising IFN and HPBCD, wherein the HPBCD is present at about 500-fold to about 700-fold molar excess with respect to said IFN, and that the previous office action failed to establish that the HPBCD concentration is a result-effective variable, and thus it cannot be optimized via routine experimentation. The Applicant also argues that the claims of the present invention are not obvious in view of Shirley and Dorin because this combination does not teach each and every limitation of the claims. Specifically, the Applicants argue that Shirley and Dorin fail to teach an IFN composition comprising HPBCD at about 500-fold to about 700-fold molar excess with respect to the IFN. The Applicant also asserts that neither Shirley nor Dorin provides the motivation to create an IFN formulation comprising a second antioxidant, such as HPBCD, and no reasoning to do so is provided in the previous office action.

These arguments have been fully considered and are not persuasive. Regarding Applicants arguments that the HPBCD amount is not a result-effective variable, it is noted that Dorin teaches that HPBCD is a known protectant of polypeptides, and helps prevent oxidation, aggregation, chemical linkage, and degradation of polypeptides (see above). Furthermore, regarding protectants such as HPBCD, Dorin teaches "too much amorphous protectant will hinder efficient lyophilization, and too little will reduce the shelf-life of the lyophilized product" (column 13, lines 29-31). Therefore, it would be expected that determining the most effective amount of HPBCD would be critical in the formulation of a pharmacologically useful IFN formulation, and because HPBCD is indeed a result-effective variable, it would be obvious to optimize the concentration or amount via routine optimization.

Regarding Applicants arguments that the combination of Shirley and Dorin do not teach each and every limitation of the claims, namely the HPBCD amount, it is noted that while Dorin does not specifically teach the recited amounts, it would be obvious to optimize the HPBCD amount or concentration in the claimed formulation because, as discussed in the preceding paragraph, HPBCD is indeed a result-effective variable.

Regarding Applicants arguments that the combination of Shirley and Dorin do not provide the motivation to add a second antioxidant, such as HPBCD, to the IFN formulation of Shirley, it is noted that both Shirley and Dorin teach the necessity of antioxidants in the formulation of pharmaceutical compositions of IFNs. As taught by Shirley, and quoted by the Applicant on page 16 of the 10/14/2009 response, "The stabilization of polypeptides in pharmaceutical compositions remains an area in which trial and error plays a major role.....Excipients that are added to polypeptide pharmaceutical formulations to increase their stability include buffers, sugars, surfactants, amino acids, polyethylene glycols, and polymers, but the stabilizing effects of these chemical additives vary depending on the protein". In reading this passage, a person of ordinary skill in the art might conclude that not all surfactants, buffers, protectants/antioxidants, etc would effectively stabilize a composition comprising IFN. However, because Shirley and Dorin provide a description of excipients which are compatible with IFN stabilization, including antioxidants such as HPBCD and EDTA, the skilled artisan would be lead to formulate IFNs with these excipients. Furthermore, because a skilled artisan would know that both HPBCD and EDTA are result-effective variables which are effective towards the same purpose (stabilization by prevention of oxidation), one would know that they are interchangeable, or alternatively, would suspect that a formulation comprising both EDTA and HPBCD would be effectively protected from oxidation. *In re Kerkhoven* (205 USPQ 1069, CCPA 1980) summarizes:

"It is *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for the same purpose in order to form a combination that is to be used for the very same purpose: the idea of combining them flows logically from their having been individually taught in the prior art."

2. Claims 12, 20, 23, 32-35 and 37 *remain rejected*, and new claims 38 and 42-44 are also rejected under 35 USC § 103(a) as being obvious in view of Shirley *et al* ("Shirley" – US 20020172661) and Dorin *et al* ("Dorin" – US 5,814,485), and further in view of Chen et al (US 6,569,420) as set forth on pages 7-8 of the office action mailed on 6/23/2009.

The subject matter of the presently claimed invention is discussed above. Claims 12 and 23 are further drawn to the stabilized pharmaceutical composition of claim 1, wherein the antioxidant is methionine, while claim 20 recites the composition of claim 1 with the specific bacteriostatic agent benzyl alcohol. Claims 32-35 and 37 are drawn to an article of manufacture comprising stabilized liquid pharmaceutical composition comprising an IFN, including recombinant IFN-β, and a buffer such as acetate buffer, 2-hydroxypropyl-beta-cyclodextrin, an isotonicity agent such as mannitol, an anti-oxidant such as methionine, and a bacteriostatic agent such as benzyl alcohol, and a hermetically sealed container

comprising said composition. Also claimed is an article of manufacture wherein said container is for mono-dose, including a pre-filled syringe for mono-dose administration, a vial, or a kit comprising said pharmaceutical composition and a bacteriostatic agent. New claims 38 and 42-44 are drawn to an article of manufacture comprising a container for multidose administration (claim 38), and specific formulations comprising IFN-β-1a, HPBCD, methionine, and mannitol, optionally in an acetate buffer and in a contianer.

The disclosures of Shirley and Dorin are discussed above. Shirley further teaches stabilized liquid IFN-β formulations in sealed vials suitable for unit-dose or multi-dose (paragraph 0074), and specifically teaches liquid formulations in pre-filled syringes for single-dose or multi-dose administration (paragraph 0048). Neither Shirley nor Dorin specifically teach a stabilized composition comprising IFN-β comprising methionine and/or benzyl alcohol. However, Chen teaches that IFN compositions can be formulated using both methionine and benzyl alcohol (column 39, line 65 - column 40, line 1).

In the response received on 10/14/2009, the Applicant argues that the combination of Shirley and Dorin fails to establish a *prima facie* case of obviousness for the claimed invention because there is no teaching that the concentrations of HPBCD, mannitol, EDTA, acetate buffer, and/or bacteriostatic agents were recognized as result-effective variables, and furthermore, Shirley and Dorin do not teach each and every limitation of the claims, such as the HPBCD concentration. These deficiencies are not remedied by Chen.

The Applicant also asserts that the previous office action provides no rational as to why the combination of Shirley, Dorin, and Chen would provide any motivation to add a third anti-oxidant (such as methionine) to the composition arising from Shirley and Dorin.

These arguments have been fully considered and are not persuasive. As discussed above, HPBCD is a result-effective variable, and it would be obvious to optimize the HPBCD concentration/amount in an IFN composition. Similarly, mannitol, EDTA, acetate buffer, and bacteriostatic agents would also be expected to be result-effective variables because the proper amount or concentration of these agents in a formulation is critical to the overall properties of the formulation. For example, the optimal amount of bacteriostatic reagent(s) would be required to effectively prevent microbial growth or contamination in a pharmaceutical composition, while the proper amounts of mannitol, EDTA, and acetate buffer would be required to maintain the isotonicity and proper pH of the formulation, and to prevent aggregation/oxidation. Because too little of these agents would be insufficient to maintain the most effective formulation, and too much could lead to unwanted effects or toxicity, these agents are result-effective variables which would be obvious to optimize.

Regarding Applicants arguments that the combination of Shirley, Dorin, and Chen does not provide motivation to add a third anti-oxidant, such as methionine, it is noted that Shirley, Dorin, and Chen provide a description of excipients which are compatible with IFN stabilization, including the antioxidants HPBCD, EDTA, and methionine, providing a person of ordinary skill in the art the motivation to formulate IFNs with these antioxidants. Furthermore, because a skilled artisan would know that HPBCD, EDTA, and methionine are result-effective variables which are effective towards the same purpose (stabilization by prevention of oxidation), one would know that they are interchangeable, or alternatively, would suspect that a formulation comprising various combinations, including all three antioxidants, would be effectively protected from oxidation.

3. Claim 36 *remains rejected* under 35 USC § 103(a) as being obvious in view of Shirley *et al* ("Shirley" – US 20020172661) and Dorin *et al* ("Dorin" – US 5,814,485), and further in view of Chen et al (US 6,569,420), and further in view of Tsals et al ("Tsals" – US 5,858,001) as set forth on pages 8-9 of the office action mailed on 6/23/2009.

The subject matter of the present invention and the disclosures of Shirley, Dorin, and Chen are discussed above. Claim 36 is further drawn to an article of manufacture comprising the claimed pharmaceutical IFN composition in a container for mono-dose administration, wherein said container is a cartridge for an auto-injector.

Shirley, Dorin, and Chen are silent regarding an article of manufacture comprising the claimed composition and a container, wherein said container is a cartridge for an auto-injector. However, Tsals teaches a cartridge-based drug delivery device that is an auto-injector comprising a cartridge that serves as a reservoir (see abstract; claim 1). Tsals also teaches that this device is suitable for administration of IFN formulations, including IFN-α, -β, and -γ (column 7, lines 4-9).

In the response received on 10/14/2009, the Applicant argues that the claimed invention is not obvious in view of the combination of Shirley, Dorin, Chen, and Tsals because this combination does not teach each and every limitation of the claimed invention. The Applicants assert that the cited combination of art does not teach that the concentrations of HPBCD, mannitol, EDTA, acetate buffer, and/or bacteriostatic agents were recognized as result-effective variables, and there is no teaching of suggestion of a composition comprising HPBCD at 500-fold to about 700-fold molar excess with respect to IFNs present within the composition. Additionally, the Applicant argues that there is no teaching or

suggestion of adding a second and/or third antioxidant to the composition of Shirley, and that Tsals fails to remedy these defects.

These arguments have been fully considered and are not persuasive. As set forth above, the concentration of HPBCD, mannitol, EDTA, acetate buffer, and/or bacteriostatic agents would be expected to be result-effective variables, and thus it would be obvious to optimize the concentration of these agents in the claimed formulation. Furthermore, as set forth above, it would be obvious to add antioxidants such as HPBCD or methionine to the composition of Shirley because a skilled artisan would know that each of these antioxidants is effective for stabilizing IFNs.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Rejection of claims 1-15, 17-23, 25, and 32-37 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 32-45, 48-57, and 60-61 of commonly-owned and copending Application No. 11/597,987, as set forth on pages 10-11 of the office action mailed on 6/23/2009, is *withdrawn* in view of Applicants cancellations of the claims of the '987 application and submission of new claims 64-65, which are drawn to an IFN-β formulation comprising IFN-β, lysine, methionine, poloxomer 188, and an aqueous acetate buffer, rather than a formulation comprising IFN-β, HPBCD, an acetate buffer, mannitol, and/or an aqueous buffer, as is currently claimed.

2. Claims 1-15, 17-23, 25, and 32-37 *remain provisionally rejected*, and new claims 38-44 are also rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 5-8, 10-16, and 18-33, as well as new claims 34-39, of commonly-owned and copending Application No. 10/554,602, in view of Dorin *et al*, as set forth on pages 9-10 of the office action mailed on 6/23/2009.

In the response received on 10/14/2009, the Applicants argue that there was no articulated reasoning in the last office action as to why the claims of the '602 application are obvious variants of the claims of the instant application. Specifically, the Applicant argues that there is no reasoning as to why a person of ordinary skill in the art would be motivated to add a second anti-oxidant, such as HPBCD, to the composition of the '602 claims, and no reasoning as to why a skilled artisan would then be motivated to add HPBCD to the composition of the '602 claims in the molar ratios claimed in the present application (about a 500-fold to about a 700-fold molar excess with respect to the IFN present in the composition).

These arguments have been fully considered and are not persuasive. As set forth above, Dorin teaches that HPBCD is an antioxidant that is effective for stabilization of IFNs, and thus a person of ordinary skill in the art would know that that both methionine and HPBCD are effective towards the same purpose (stabilization of IFN formulations by preventing oxidation of IFN), and would therefore recognize that these excipients are interchangeable, or alternatively would suspect that a formulation comprising both methionine and HPBCD would be effectively protected from oxidation. Furthermore, given the importance of stabilization of protein formulations, such as IFN formulation, one of ordinary skill in the art would know that too little of either methionine or HPBCD would be insufficient to stabilize said IFN, while too much could result in unwanted side-effects and/or toxicity. Therefore, a person of ordinary skill in the art would recognize HPBCD as a result-effective variable, and would have the motivation to optimize the concentration of HPBCD in an IFN formulation.

***Conclusion***

No claim is allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571)272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bruce D. Hissong
Art Unit 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647